Prevalence of rare mitochondrial DNA mutations in mitochondrial disorders

Titre	Prevalence of rare mitochondrial DNA mutations in mitochondrial disorders
Type de publication	Article de revue
Auteur	Bannwarth, S. [1], Procaccio, Vincent [2], Lebre, Anne-Sophie [3], Jardel, C. [4], Chaussenot, A. [5], Hoarau, C. [6], Maoulida, H. [7], Charrier, N. [8], Gai, X. [9], Xie, H. M [10], Ferré, Marc [11], Fragaki, K. [12], Hardy, G. [13], Mousson de Camaret, Bénédicte [14], Marlin, S. [15], Dhaenens, C. M [16], Slama, A. [17], Rocher, C. [18], J. Bonnefont, Paul [19], Rotig, Agnès [20], Aoutil, N. [21], Gilleron, M. [22], Desquiret-Dumas, Valérie [23], Reynier, Pascal [24], Ceresuela, J. [25], Jonard, L. [26], Devos, A. [27], Espil-Taris, C. [28], Martinez, Delphine [29], Gaignard, P. [30], Sang, K. HLe Quan [31], Amati-Bonneau, Patrizia [32], Falk, M. J [33], Florentz, C. [34], Chabrol, Brigitte [35], Durand-Zaleski, Isabelle [36], Paquis-Flucklinger, V. [37]
Editeur	BMJ Publishing Group
Type	Article scientifique dans une revue à comité de lecture
Année	2013
Langue	Anglais
Date	2013
Numéro	10
Pagination	704 - 14
Volume	50
Titre de la revue	Journal of medical genetics
ISSN	1468-6244
Mots-clés	Adolescent [38], Adult [39], Age of Onset [40], Aged [41], Child [42], Child, Preschool [43], DNA, Mitochondrial/genetics [44], Female [45], Humans [46], Infant [47], Infant, Newborn [48], Male [49], Middle Aged [50], Mitochondrial Diseases/diagnosis/epidemiology/genetics [51], Mutation [52], Phenotype [53], Prevalence [54], Young Adult [55]

Résumé en anglais	BACKGROUND: Mitochondrial DNA (mtDNA) diseases are rare disorders whose prevalence is estimated around 1 in 5000. Patients are usually tested only for deletions and for common mutations of mtDNA which account for 5-40% of cases, depending on the study. However, the prevalence of rare mtDNA mutations is not known. METHODS: We analysed the whole mtDNA in a cohort of 743 patients suspected of manifesting a mitochondrial disease, after excluding deletions and common mutations. Both heteroplasmic and homoplasmic variants were identified using two complementary strategies (Surveyor and MitoChip). Multiple correspondence analyses followed by hierarchical ascendant cluster process were used to explore relationships between clinical spectrum, age at onset and localisation of mutations. RESULTS: 7.4% of deleterious mutations and 22.4% of novel putative mutations were identified. Pathogenic heteroplasmic mutations were more frequent than homoplasmic mutations (4.6% vs 2.8%). Patients carrying deleterious mutations showed symptoms before 16 years of age in 67% of cases. Early onset disease (<1 year) was significantly associated with mutations in protein coding genes (mainly in complex I) while late onset disorders (>16 years) were associated with mutations in tRNA genes. MTND5 and MTND6 genes were identified as 'hotspots' of mutations, with Leigh syndrome accounting for the large majority of associated phenotypes. CONCLUSIONS: Rare mitochondrial DNA mutations probably account for more than 7.4% of patients with respiratory chain deficiency. This study shows that a comprehensive analysis of mtDNA is essential, and should include young children, for an accurate diagnosis that is now accessible with the development of next generation sequencing technology.
URL de la notice	http://okina.univ-angers.fr/publications/ua8375 [56]
DOI	10.1136/jmedgenet-2013-101604 [57]
Lien vers le document	http://dx.doi.org/10.1136/jmedgenet-2013-101604 [57]
Titre abrégé	J Med Genet

Liens

[1] http://okina.univ-angers.fr/publications?f[author]=14676
[2] http://okina.univ-angers.fr/v.procaccio/publications
[3] http://okina.univ-angers.fr/publications?f[author]=25539
[4] http://okina.univ-angers.fr/publications?f[author]=14678
[5] http://okina.univ-angers.fr/publications?f[author]=14679
[6] http://okina.univ-angers.fr/publications?f[author]=14680
[7] http://okina.univ-angers.fr/publications?f[author]=14681
[8] http://okina.univ-angers.fr/publications?f[author]=14682
[9] http://okina.univ-angers.fr/publications?f[author]=14352
[10] http://okina.univ-angers.fr/publications?f[author]=14337
[11] http://okina.univ-angers.fr/marc.ferre/publications
[12] http://okina.univ-angers.fr/publications?f[author]=14683
[13] http://okina.univ-angers.fr/publications?f[author]=14684
[14] http://okina.univ-angers.fr/publications?f[author]=24198
[15] http://okina.univ-angers.fr/publications?f[author]=14233
[16] http://okina.univ-angers.fr/publications?f[author]=14686
[17] http://okina.univ-angers.fr/publications?f[author]=1230
[18] http://okina.univ-angers.fr/publications?f[author]=14687
[19] http://okina.univ-angers.fr/publications?f[author]=14688
[20] http://okina.univ-angers.fr/publications?f[author]=1069

[21] http://okina.univ-angers.fr/publications?f[author]=14689
[22] http://okina.univ-angers.fr/publications?f[author]=14690
[23] http://okina.univ-angers.fr/valerie.desquiretdumas/publications
[24] http://okina.univ-angers.fr/pascal.reynier/publications
[25] http://okina.univ-angers.fr/publications?f[author]=14691
[26] http://okina.univ-angers.fr/publications?f[author]=14692
[27] http://okina.univ-angers.fr/publications?f[author]=14693
[28] http://okina.univ-angers.fr/publications?f[author]=14694
[29] http://okina.univ-angers.fr/publications?f[author]=14695
[30] http://okina.univ-angers.fr/publications?f[author]=14696
[31] http://okina.univ-angers.fr/publications?f[author]=14697
[32] http://okina.univ-angers.fr/patrizia.bonneau/publications
[33] http://okina.univ-angers.fr/publications?f[author]=14353
[34] http://okina.univ-angers.fr/publications?f[author]=14698
[35] http://okina.univ-angers.fr/publications?f[author]=18825
[36] http://okina.univ-angers.fr/publications?f[author]=16460
[37] http://okina.univ-angers.fr/publications?f[author]=970
[38] http://okina.univ-angers.fr/publications?f[keyword]=1214
[39] http://okina.univ-angers.fr/publications?f[keyword]=1002
[40] http://okina.univ-angers.fr/publications?f[keyword]=6086
[41] http://okina.univ-angers.fr/publications?f[keyword]=1072
[42] http://okina.univ-angers.fr/publications?f[keyword]=1216
[43] http://okina.univ-angers.fr/publications?f[keyword]=1534
[44] http://okina.univ-angers.fr/publications?f[keyword]=12971
[45] http://okina.univ-angers.fr/publications?f[keyword]=1075
[46] http://okina.univ-angers.fr/publications?f[keyword]=991
[47] http://okina.univ-angers.fr/publications?f[keyword]=3233
[48] http://okina.univ-angers.fr/publications?f[keyword]=3235
[49] http://okina.univ-angers.fr/publications?f[keyword]=968
[50] http://okina.univ-angers.fr/publications?f[keyword]=5941
[51] http://okina.univ-angers.fr/publications?f[keyword]=13761
[52] http://okina.univ-angers.fr/publications?f[keyword]=1133
[53] http://okina.univ-angers.fr/publications?f[keyword]=1491
[54] http://okina.univ-angers.fr/publications?f[keyword]=1081
[55] http://okina.univ-angers.fr/publications?f[keyword]=6036
[56] http://okina.univ-angers.fr/publications/ua8375
[57] http://dx.doi.org/10.1136/jmedgenet-2013-101604